Remarks

In response to the restriction requirement dated June 15, 2007, Applicants elected Group I, claims 1-18, and 31-33, directed to a method of prolonging expression of a heterologous gene encoding a prodrug activating enzyme and method of increasing concentration of a chemotherapeutic drug in the vicinity of a target cell in a mammal.

Accordingly, Applicants have amended the presently pending claims to comply with the restriction requirement by cancelling the non-elected claims 19-30, and 34-36 without prejudice.

Applicants have further amended claim 1 to comply with the restriction requirement. Consequently, claim 2 has been cancelled and claim 3 amended to comply with the amendment.

Applicants have added new claim 37 directed to a vector system with two different vectors. Support for this amendment can be found, for example, in paragraph [0101] of the specification. Applicants have further added new claim 38, directed to a method of increasing the concentration of a chemotherapeutic drug in, or in the vicinity of a target malignant cell in a mammal affected with malignant cell. Support for the amendment can be found, for example in the originally filed claims 4 and 11.

Accordingly, Applicants submit that the amendments are either clerical or supported by the specification and the new claims are supported by the specification as filed and therefore do not introduce new matter. Entry of the amendments and new claims is respectfully requested.

The Examiner rejected claims 1, 19, 21 and 23-24 under 35 U.S.C. §102(b) as allegedly anticipated by Bilbao et al. (WO 99/55382) ("Bilbao").

Applicants respectfully disagree and submit that the rejection be withdrawn for the following reasons.

Bilbao does not teach a cell being transfected with a prodrug activating enzyme **and** also an anti-apoptotic agent as required by claim 1.

Accordingly, the rejection of claim 1 under 35 U.S.C. §102(b) over Bilbao should be withdrawn.

The Examiner also rejected claims 1, 19, 23-24, and 29-30 under 35 U.S.C. §102(e) as allegedly anticipated by Wilson et al. (U.S. Patent Application Publication No. 2002/0131961)("Wilson").

Applicants respectfully disagree and submit that the rejection be withdrawn for the following reasons.

Wilson does not teach a cell being transfected with a prodrug activating enzyme **and** an **anti-apoptotic agent** as required by claim 1 as directed to currently elected Group I.

Accordingly, the rejection of claim 1 under 35 U.S.C. §102(e) over Wilson should be withdrawn.

The Examiner further rejected claims 1, 19, and 23-24 under 35 U.S.C. §102(a) as allegedly anticipated by Luo et al. ("Luo").

Applicants respectfully disagree and submit that the rejection be withdrawn for the following reasons.

Luo does not teach a cell being transfected with both a prodrug activating enzyme **and** an anti-apoptotic agent.

Accordingly, the rejection of claim 1 under 35 U.S.C. §102(a) over Luo should be withdrawn.

The Examiner rejected claims 1-13, 19, 21, 23-24, and 29-30 under 35 U.S.C. §103(a) as allegedly obvious over Waxman et al. (WO 99/05299)("Waxman") in view of Bilbao.

Applicants respectfully submit that the rejection be withdrawn for the following reasons.

The Examiner contended that Waxman can be combined with Bilbao because Bilbao states that one would look at other methods to prolong the expression of transgenes. The problem with the Examiner's analysis is that it is directly contradictory to the approach of Waxman (see, Declaration by Dr. David Waxman ("Declaration") attached herewith). Indeed, the Examiner acknowledged that Waxman teaches that the gene transfer system can be used together with, among other agents, **apoptotic agents** (see, page 7, of the August 8, 2007 Office Action). Waxman teaches use of apoptotic agents, **not** use of **anti**-apoptotic agents. Thus Waxman is looking at the direct opposite of the present invention. Therefore, a skilled artisan would not have been looking to Waxman to modify Bilbao (see, Declaration).

The combination certainly does not teach or suggest that one would use a neoplastic cell in this method (see claims 4 and new claim 38). Rather, the combination teaches against using such a cell.

Accordingly, the rejection of claims 1-13, 19, 21, 23-24, and 29-30 under 35 U.S.C. §103(a) over Waxman in view of Bilbao should be withdrawn.

The Examiner rejected claims 14-18 and 31-33 under 35 U.S.C. §103(a) as allegedly obvious over Waxman in view of Bilbao and further in view of Robertson et al. (U.S. Patent No. 6,709,866)("Robertson") and Griffith et al (U.S. Patent No. 6,900,185)("Griffith").

Applicants respectfully disagree and submit that the rejection be withdrawn for the following reasons.

As explained above, and in the Declaration, Waxman teaches not to use an apoptosis **inhibitor**—and use an apoptosis **inducer** instead. The exact opposite. Neither Robertson nor Griffith provides the motivation to use anti-apoptotic gene in the method of Waxman instead of an apoptotic gene. The Examiner also acknowledges that Griffith specifically teaches using apoptosis **inducers**, **not** apoptosis **inhibitors** (page 11, 2nd full par., of the August 8, 2007 Office Action). Thus, the combination teaches the opposite—using apoptosis inducers—and teaches against the present claimed invention.

Accordingly, the rejection of claims 14-18 and 31-33 under 35 U.S.C. §103(a) Waxman in view of Bilbao and further in view of Robertson and Griffith should be withdrawn.

Claims 1-6 were also rejected under 35 U.S.C. §103(a) as allegedly obvious over Waxman in view of Bilbao and further in view of Beidler et al.

Applicants respectfully disagree and submit that the rejection be withdrawn for the following reasons.

As discussed above, Waxman teaches that one can combine their method with apoptosis **inducers**, not **inhibitors**, and there is nothing in Beidler that rebuts this. Beidler merely describes that p35 functions as an apoptosis inhibitor. Therefore, there would be no motivation for a skilled artisan to combine Beidler with Waxman.

The combination certainly teaches against using a neoplastic cell (see claims 4 and 38) because it teaches and suggests that with neoplastic cells one needs to use an apoptosis **inducer**.

Accordingly, the rejection of claim 1-6 under 35 U.S.C. §103(a) over Waxman in view of Bilbao and further in view of Beidler should be withdrawn.

In view of the foregoing amendments, arguments and evidence, Applicants respectfully submit that all claims are in condition for allowance. Early and favorable action is requested.

The Applicants believe no fees are due at this time. However, in the event that any additional fees are required, the Commissioner is authorized to charge Nixon Peabody LLP Deposit Account No. 50-0850.

Respectfully submitted,

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